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WR279396: A Phase II Study in the Old World

PRINCIPAL INVESTIGATOR: Pierre A. Buffet, M.D., Ph.D.

CONTRACTING ORGANIZATION: Centre de recherche Clinique Institut de Paris
75015 Paris, France

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6. AUTHOR(S) :

Pierre A. Buffet, M.D., Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)Centre de recherche Clinique Institut de Paris
75015 Paris, France

Email: pabuffet@pasteur.fr

**8. PERFORMING ORGANIZATION
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Paris, July, 14, 2002

**Annual Report the project for "Topical Treatment of
Cutaneous Leishmaniasis
with the WR 279396 A phase 2 study in the Old World"**

Abstract

Action was taken in three directions

1 - Coordination between sites. The French Study Coordinator visited the Tunisian site (April). The Tunisian Study Coordinator visited the French site (July). Team members involved were identified. The protocol and SOPs were improved. A contract was raised between the Institut Pasteur in Paris and the Institut Pasteur in Tunis to define money transfers and responsibilities.

2 - Regulatory issues Approval from the Local Tunisian Ethical Comity was obtained. Approval from Tunisia Ministry of Health is ongoing. In France, the second submission to the French IRB will be sent on July 16th 2002. A first-step approval from the French commission for computerized data handling was obtained (2d of July). The second step should be completed before August 8th 2002. The project was submitted to the AFSSAPS (French equivalent of the F.D.A). Final approval depends on the French IRB approval (end of August). A contracted company (CREAPHARM) will import the study product from the United States to France. A Federal Wide Assurance for Subjects Protection was signed (7th of July).

3 - Site set-up. Clinical laboratories, at both sites, were identified.

Conclusion If regulatory agencies in France and Tunisia keep on schedule, all regulatory approvals should be obtained before the end of September. The first inclusion should take place at the beginning of October 2002.

Summary 14/07/02

Annual Report the project for "Topical Treatment of Cutaneous Leishmaniasis with the WR 279396 A phase 2 study in the Old World"

1 - Coordination between sites. The French Study Coordinator visited the Tunisian site (April). The Tunisian Study Coordinator visited the French site (July). Team members involved were identified. The protocol and SOPs were improved. A contract was raised between the Institut Pasteur in Paris and the Institut Pasteur in Tunis to define money transfers and responsibilities.

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Report of year 1:

1/ Visit to the Tunisian site by the PI (Max Grögl), QA/QC specialist (Jane Cook), Medical systems product manager (Erich Lenhert) and the French Co Pi (Pierre Buffet) : 10 to 13 April 2002

The visit permitted to present the trial to the General Director of the Pasteur Institute of Tunis (Prof. Koussay Dellagi) who expressed his full support to the project. The files related to the project were presented by the Pi and discussed. Dr. H. Louzir accepted to act as a clinical monitor for the trial instead of Dr. R. Ben Ismail who will be abroad during the trial.

A site visit to the endemic area of Sidi Bouzid where patients will be recruited in Tunisia, took place on the 12 th of April 2002. A visit to the regional directorate of Health with : Dr. Max Groggl, Erich Lehnert, Dr. Pierre Buffet, Jane Cook, Dr. Afif Ben Salah and Mr. Amor Zaatour permitted to explain the context, the objectives and the procedures of the trial to regional health authorities. The visiting team with the regional team: Dr. Zaher El Ahmadi (Regional chief of Primary Health Care) and Mr. Zaafour (Regional supervisor) went to the regional hospital of Sidi Bouzid and interviewed the technicians of the laboratory regarding different biological tests and their quality control. In addition the team visited two primary health care centers where cutaneous leishmaniasis patients will be included . They consulted the clinical records, interviewed the nurses and evaluated the recruitment potential

of these centres.

The budget of the project was adjusted according to the real needs as assessed by the American team and the Co-PIs (Dr. Pierre Buffet and Dr. Afif Ben Salah) after the site visit.

2/ Administrative and organisational aspects related to the project in Tunisia

The Tunisian Co-PI submitted the protocol to the IRB of Pasteur Institute of Tunis in January 2002. He had three meetings to explain all ethical issues related to the trial. The IRB recommended some changes related to the facial location of lesions with a disfiguring potential and to exclude females aged 18 to 45 years to prevent the risk of pregnancy. When the IRB gave the agreement, an official letter explaining the objectives of the trial was sent to the Tunisian Minister of Health in order to obtain the authorization of the Ministry of Health to commence the trial. The Ministry of Health replied and required the following documents to permit the achievement of the trial:

- 1- The protocol
- 2- The contract signed by the different partners
- 3- The informed consent
- 4- All documents to be signed by the patients
- 5- A formal agreement of the scientific council of Institut Pasteur de Tunis
- 6- A letter specifying the date of onset of the trial as well as the different centers involved has to be written.

Therefore, the General Director of Institut Pasteur asked the scientific council of the Institute to meet and the Tunisian Co-PI presented the trial, explained the protocol and all the steps already achieved including the modifications recommended by the IRB. The scientific council approved the trial. A copy of the meeting minutes will be sent to the Ministry of Health.

All required remaining documents are in the process of preparation including a translated version to Arabic of the informed consent (ready) and a contract between Institut Pasteur in Paris and Institut Pasteur of Tunis (almost ready).

3/ Administrative and organisational aspects related to the project in France

In France, the second submission to the French IRB will be sent on July 16th 2002. Answers were provided to all questions from the French IRB. More comments were added taking in account the modifications asked for by the Tunisian IRB.

A first-step approval from the French commission for computerized data handling was obtained (2d of July). The second step should be completed before August 8th 2002.

The project was submitted to the AFSSAPS (French equivalent of the F.D.A). Final approval depends on the French IRB approval (end of August).

A Federal Wide Assurance for Subjects Protection was signed (7th of July).

A private company was contracted to perform the import of the product (WR279396). By Law the Institut Pasteur is not allowed to import pharmaceutical products.

Conclusion If regulatory agencies in France and Tunisia keep on schedule, all regulatory approvals should be obtained before the end of September. The first inclusion should take place at the beginning of October 2002.

Up-dating :

Administrative and organisational aspects related to the project in France after July

Final approval of French IRB obtained le 29/08/02.

A second and final step approval from the French commission for computerized data handling was obtained le 13/09/02.

Final approval of AFSSAPS (French equivalent of FDA) obtained le 17/09/02.

Approval of FWA Assurance : N° = FWA00003327 - Type = F

The importation contract of product (WR279396) is performed.